REMARKS

I. Status of Claims

Claims 15 and 16 are pending in the application. No claim amendments are made herein.

II. Interview Summary

Applicants thank the Examiner for the telephone interview on May 19, 2011. As set forth in the Interview Summary mailed by the Office, during the interview Applicants' representatives explained the presently claimed invention in detail, pointed out the differences between the cited art and the invention, and further explained why one of skill in the art would not have been motivated to use the pairwise distribution function (PDF) of Bizid in the methods of Lemmo.

III. Rejection Under 35 USC § 103

Claims 15 and 16 have been rejected in the Office Action under 35 USC §103(a) as allegedly obvious over US Patent Application Publication No. 2003/0123057 to Lemmo ("Lemmo") in view of "Structure by diffraction of X-rays of liquid gallium between +50 and –110 °C," Physica Status Solid A, 23(1); 135-145 (1974) to Bizid et al. ("Bizid"). Office Action, pages 3-5. According to the Office, "since both Lemmo et al. and Bizid et al. employ X-ray diffraction for the analysis of sample structure, it would have been obvious to one of ordinary skill in the art to employ PDF with X-ray diffraction analysis for the purpose of comparing forms of a sample such as liquid and crystalline forms

(English Abstract of Bizid et al.). Applicants disagree, and therefore respectfully traverse the rejection.

As the Office is aware, it is necessary to look at Applicants' claimed invention **as a whole** to determine whether the invention would have been obvious. MPEP § 2141.02. Further, a prior art reference must also be considered **as a whole**, including portions of the reference that would **lead one of skill of art away from** the claimed invention. *See, e.g.* MPEP § 2141.02, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). And, importantly, in determining the differences between the prior art and the claims, the question is not whether the differences would have been obvious, but whether the **claimed invention as a whole** would have been obvious. MPEP § 2141.02; *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983).

Further, when considering whether a proposed modification of prior art references would have been obvious at the time of the invention, there must have been some "apparent reason to combine the known elements in the fashion claimed by the patent at issue," citing *KSR Int'l Co. v. Teleflex Inc.*,127 S. Ct. 1727, 1741 (2007). The Office can establish such a reason, for example, by showing some motivation or suggestion to modify the prior art teachings. *Id.* However, regardless of the standard used by the Office, there must be a clear articulation on the record of the reason why the claimed invention would have been obvious.

As Applicants' representatives explained during the interview, the claimed invention is directed to determining the residual crystallinity in a substance. Applicants have invented a method whereby the PDF can determine whether a substance which is

purportedly amorphous or otherwise disordered, contains residual crystallinity. The method recited in the current claims provides a significant advantage to the field of use of PDF, as it was not previously known. Neither Bizid nor Lemmo, nor the combination thereof, render the claimed method obvious, at least because Bizid actually **teaches away from** the claimed methods, and further because there would have been no motivation to combine the teachings of Lemmo and Bizid, as set forth below.

Bizid teaches that the radial distribution function, which is the PDF, can be used to show differences in structure between liquid gallium and crystalline gallium. Bizid is written in French with an English abstract. That abstract, in its entirety, is reproduced below:

> An X-ray diffraction study is carried out on liquid gallium between temperatures of +50 and –110 °C. It is observed on the diffracted intensity patterns that a secondary peak, associated with the main peak, becomes more and more important as the temperature decreases. The radial distribution functions do not indicate, however, any notable change with the temperature, i.e. the nearest neighbours number and the maxima position do no change significantly. The comparison of pair distribution functions of liquid gallium and crystalline phases, the structures of which are known, shows that the atomic distribution in the liquid presents more marked analogies with the atomic distributions of metastable crystalline forms than with that of stable form.

The teachings of Bizid show a study on a unitary sample of gallium as the material is cooled to well below its freezing point (gallium has melting point of about 30°C, as stated on Wikipedia). As the material cools, the authors note a change in the x-ray diffraction signal, but fail to see any change in the corresponding PDF. In other words, the PDF was an **insensitive** measure of gallium changes when compared with the usual x-ray diffraction techniques. Accordingly, to one of ordinary skill in the art

when considering whether to use the PDF function to distinguish between different solid phases of, for example a pharmaceutical, Bizid **teaches away from** using the PDF function because it discloses that x-ray diffraction is more sensitive than the PDF and, indeed, PDF did not reveal any difference in gallium. When considering this conclusion, one of skill in the art would have understood that PDF was not a useful technique in this regard, and thus, would not have been motivated to use it in the way the present invention does.

For completeness, Applicants note that the Abstract also teaches that when comparing the PDF of liquid gallium to metastable crystalline forms of gallium, the authors observed similarities between the metastable crystalline form and the liquid form. While the authors do not describe what they mean by a metastable crystalline form, they do distinguish it from the crystalline forms including the "stable" form. In sum, therefore, Bizid teaches that the PDF of liquid gallium looks like that of a metastable crystalline gallium and that analysis of gallium in a temperature study is insensitive to the PDF method. While the similarities of these two particular phases of gallium are immaterial to this invention, the insensitivity of PDF in the gallium system is a significant teaching away from the present invention.

Applicants note that, in contrast to Bizid, the instant invention relies on the PDF to help identify residual crystallinity of a material that is substantially amorphous or disordered by comparing PDFs of the sample to be tested and that of a crystalline form. Nowhere in Bizid is there the concept of residual crystallinity and there is no suggestion that the PDF could be used to find residual crystallinity. Indeed, since Bizid teaches that PDF is insensitive to changes readily picked up by x-ray diffraction, it clearly follows

that the PDF would not be used to find residual crystallinity in a sample of liquid gallium. Further, the fact that a metastable form and a liquid form are similar has no bearing on the claims because the claims are directed to detecting crystalline forms which, by their very nature, differ than amorphous forms. Indeed, Applicants have determined that they can use PDF to perform this function in pharmaceuticals, something Bizid does not teach or suggest. Thus, when considering both the present invention and Bizid, each as a whole, one of skill in the art would consider, one of skill in the art would consider Bizid as a **teaching away from** using the PDF to find residual crystallinity in any other substance such as an amorphous or otherwise disordered pharmaceutical.

Lemmo adds nothing to the analysis. There is no mention or suggestion of the PDF or radial distribution function, and references to other techniques therein are irrelevant to the claims at issue which are limited to the PDF technique. As such, one of skill in the art would not have been motivated to modify the methods of Lemmo to incorporate the PDF of Bizid, in such a way as to arrive at the presently claimed invention.

IV. Conclusion

In view of the above remarks, Applicants believe the pending claims are patentable under all applicable sections of Title 35 of the United States Code. Accordingly, Applicants request that the rejection be withdrawn, and a Notice of Allowance be promptly issued.

If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 50-4126.

Respectfully submitted,

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